Séminaire

Institut de Biologie Structurale

CONFÉRENCIER INVITÉ

Vendredi 28 Septembre 2018 à 11h

Salle des séminaires

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

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Structure determination of membrane proteins, from GPCRs to the elusive NADPH oxidases

Most protein chemists with experience on membrane proteins would agree that these proteins are troublesome. Problems can range from poor expression levels to instability in detergent solution, thus hampering efforts towards successful biophysical and structural investigations. Yet, in the past 10 years we have seen a major progress in the field, thanks to various methodological and technical advances. During the seminar I will briefly cover some of these advances taking examples from my own work over the years, including the *conformational stabilization* by mutagenesis of G protein-coupled receptors (GPCRs) that has allowed the crystallisation of several GPCRs (such as the human adenosine receptor A2a) but also neurotransmitter transporters.

More recently, our work at the University of Pavia has focused on NADPH oxidase (NOX), membrane enzymes whose function is the generation of reactive oxygen species. We described the atomic structures of the trans-membrane and NADPH-dehydrogenase domains of NOX5 from the cyanobacterium *Cylindrospermum stagnale*, a close homolog of human NOX5. The trajectory of the electrons from the intracellular side across the membrane to the oxygen is identified. The structure locates a specific binding cavity for oxygen, which is reduced through an outer-sphere mechanism. The C-terminus functions as a conformational receiver of the regulatory signals that control the ROS-producing activity of NOXs. Finally, a stabilizing mutation of the DH domain of csNOX5 can be successfully grafted onto other NOXs with beneficial effects on enzyme production. This mutation represents a valuable tool for further biochemical and structural studies of NOXs.

Hôte : Franck Fieschi (IBS/Groupe Membrane & Pathogènes)

L'accès au campus EPN nécessite un avis de rendez-vous

Contactez O. Cavoret (au moins 48h à l'avance) - T. 04 57 42 87 04 - email : ibs.seminaires@ibs.fr